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WO 2004/026330 A1

(54) **Title:** METHODS AND PREPARATIONS FOR CURING CRITICALLY ILL PATIENTS

(57) **Abstract:** The present invention pertains to the use of a blood mannan-binding lectin (MBL) regulator for the manufacture of a life saving drug to treat or cure a critically ill patient. It further involves the use of measurements of MBL to predict mortality in critically ill ICU patients. One further aspect of present invention is to the use of monomers and oligomers of MBL in prophylactic and/or curative treatment of patients admitted to intensive care units (ICUs).

Replaced by Art 19 Amd't.

METHODS AND PREPARATIONS FOR CURING CRITICALLY ILL PATIENTS

Claims

1. Use of a regulator of blood mannan-binding lectin (MBL) in the manufacture of a medicament to treat critically ill patients.
2. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to prophylactically treat critically ill patients.
3. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to ameliorate or cure critically ill patients.
4. Use of a regulator of blood MBL of claim 1, in the manufacture of a life saving drug to prophylactically treat or to cure critically ill patients.
5. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to increase the survival rate in critical ill patients.
6. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to reduce the time a critically ill patient stays, within the hospital, for example within the intense care unit .
7. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to treat or cure systemic inflammatory response syndrome (SIRS) in critically ill patients.
8. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to prevent, treat or cure critically ill patient, characterised in that the critically ill patient were previously non-immunocompromised
9. Use of a regulator of blood MBL of claim 1, in the manufacture of a medicament to reduce mortality, hospital stay, need for dialysis and need for ventilatory support in a critically ill patient.
10. ~~Use of the regulator of blood MBL according to any of the claims 1 to 9, in~~ the manufacture of a medicament to prophylactically or therapeutically treat individuals in the ICU having serum levels of MBL below 500 ng/ml.
11. Any of the claims 1 to 10, wherein the blood MBL regulator is a compound of the group of biologically active substances, which stimulate hepatocytes to synthesise and/or release of MBL .

11. Any of the claims 1 to 10, wherein the blood MBL regulator is a compound of the group of biologically active substances, which stimulate hepatocytes to synthesise and/or release of MBL .
12. Any of the claims 1 to 10, wherein the blood MBL regulator is growth hormone or a bioactive derivative thereof.
13. Any of the claims 1 to 10, wherein the blood MBL regulator is a mannan-binding lectin (MBL) polypeptide.
14. Any of the claims 1 to 10, wherein the blood MBL regulator is a composition comprising at least one mannan-binding lectin (MBL) polypeptide monomer, or at least one mannan-binding lectin (MBL) polypeptide oligomer comprising or at least one mannan-binding lectin (MBL) polypeptide monomer.
15. Any of the claims 1 to 10, wherein the composition comprises at least one mannan-binding lectin (MBL) polypeptide oligomer comprising at least one mannan-binding lectin (MBL) polypeptide monomer.
16. Any of the claims 14 to 15, wherein said oligomer is preferably selected from the group of oligomers consisting of trimers, tetramers, pentamers and/or hexamers.
17. Use of any of the claims 1 to 16, wherein the medicament is for the prevention of fatal outcome during intensive care treatment of an individual.
18. Use of any of the claims 1 to 16, wherein the "condition" is multiple organ failure
19. Use of any of the claims 1 to 16, wherein the "condition" is post-surgical critical illness.
20. Use of any of the claims 1 to 16, wherein the "condition" is post-traumatic critical illness.
21. Use of any of the claims 1 to 16, wherein the patient is a patient in need of cardiac surgery, cerebral surgery, thoracic surgery, abdominal surgery, vascular surgery, or transplantation, or a patient suffering from neurological diseases, cerebral trauma, respiratory insufficiency, abdominal peritonitis, multiple trauma, severe burns.

22. Use of any of claims 1-16 in a kit-of-parts further comprising anti-bacterial, anti-viral or anti-fungal medicament.

23. The use of the claims 13 to 16, wherein the MBL polypeptide monomer or the MBL polypeptide oligomer is produced in a native host organism.

24. The use of claim 23, wherein the native hosts organism is a human cell natively expressing the MBL polypeptide monomer or the MBL polypeptide oligomer.

25. The use of claims 13 to 16, wherein the MBL polypeptide monomer or MBL polypeptide oligomer is produced by a host organism not natively expressing an MBL polypeptide.

26. The use of claims 13 to 16, wherein the MBL polypeptide monomer or the MBL polypeptide oligomer is produced by a method comprising at least one step of recombinant DNA technology in vitro.

27. The use of any of claims 24, 25 and 26, wherein the production of the MBL polypeptide monomer or the MBL polypeptide oligomer is controlled by an expression control sequence not natively associated with MBL polypeptide expression.

28. The use of any of claims 24 to 27, wherein the MBL polypeptide monomer or the MBL polypeptide oligomer is isolated from the host organism.

29. The use of any of claims 24 to 27, wherein the MBL polypeptide monomer or the MBL polypeptide oligomer is isolated by a method comprising at least one step involving affinity chromatography.

30. The use of claim 29, wherein the affinity chromatography step is capable of isolating MBL polypeptide trimers, tetramers, pentamers and/or hexamers from a composition further comprising additional MBL polypeptide oligomers and/or MBL polypeptide monomers.

31. The use of any of claims 24 to 30, wherein the MBL polypeptide monomer and/or the MBL polypeptide oligomer is free from any impurities naturally associated with the MBL polypeptide when produced in a native host organism.

32. The use of any of the claims 13 to 21, wherein the MBL polypeptide monomer is a mammalian MBL polypeptide monomer.

33. The use of claim 32, wherein the mammalian MBL polypeptide monomer is a human MBL polypeptide monomer.

34. The use of any of the claims 13 to 21, wherein the MBL polypeptide oligomer comprises MBL polypeptide monomers according to any of claims 30 to 32.

35. The use of claims 1 to 34, wherein the medicament is administered to the individual prior to another treatment at ICUs.

36. The use of claims 1 to 34, wherein the medicament is administered to the individual simultaneously, sequentially or separately with another treatment.

37. The use of claim 1 to 34, wherein the medicament is administered to the individual prior to, during and after said other treatment.

38. The use of any of the preceding claims, wherein the treatment is a prophylactic treatment.

39. The use of any of claims 13 to 38, wherein the medicament is a booster of MBL polypeptide serum levels in an individual having MBL polypeptide serum levels below a predetermined minimum MBL polypeptide serum level.

40. The use of any of the claims 1 to 39, wherein the individual has serum levels of MBL polypeptide is below 500 ng/ml.

41. The use of any of the claims 1 to 39, wherein the individual has serum levels of MBL polypeptide below 400 ng/ml.

42. The use of any of the claims 1 to 39, wherein the individual has serum levels of MBL polypeptide below 300 ng/ml.

43. The use of any of the claims 1 to 39, wherein the individual has serum levels of MBL polypeptide below 200 ng/ml.

44. The use of any of the claims 1 to 39, wherein the individual has serum levels of MBL polypeptide below 100 ng/ml.

45. The use of any of the claims 1 to 39, wherein the individual has serum levels of MBL polypeptide below 50 ng/ml.

46. The use of any of the preceding claims, wherein serum or plasma levels of MBL polypeptide in the individual are determined by quantitative analysis.

47. The use of the claims 41 to 48, wherein the analysis comprises at least one of ELISA, TRIFMA, RIA or nephelometry.

48. Method of using a MBL polypeptide composition for preventing and/or reducing inflammation and/or death in an individual, the method comprising the steps of:

i) determining serum levels of MBL polypeptide in an individual,

ii) estimating the probability of the occurrence of intensive care complications in the individual, and optionally,

iii) administering a MBL polypeptide composition to an individual.

49. Advertising media and material and information media and material having or giving information about the indications and utilities of a regulator of blood MBL levels, preferably MBL itself or any of said regulators or their compositions described in any of the claims 1 to 48.

50. A method of selling a regulator of blood MBL levels, preferably MBL itself or any of said regulators or their compositions described in any of the claims 1 to 50 by giving information of about the indications and utilities.